10 Metal Oxides
Antimicrobial Techniques

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10.1 INTRODUCTION

Many bacteria, fungi, and viruses are becoming resistant to existing antibacterial agents. In addition, new microbial species appear for unknown reasons. Diseases caused by microorganisms have become a significant threat to the human race. This could be the result of inefficiencies in various forms affecting sustainable development. The use of antimicrobial drugs today or as a result of unsustainable development harms nature and ecosystems. The development of antimicrobial agents is necessary for the event of new diseases. Although some infectious diseases have been eradicated, many more are still creating havoc in society. Infectious diseases are the leading cause of death worldwide.

From the biblical plagues and plagues of ancient Athens to the Black Death of the Middle Ages, to the 1918 "Spanish flu" pandemic, and more recently the HIV/AIDS pandemic and COVID-19, infectious diseases have continued to appear and re-emerge in ways that defy accurate predictions. The emergence of the resurgence of some diseases like tuberculosis and cholera and the emergence of new variants creating endemic in all parts of the world have been the cause of global health

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threats [1,2]. The pathogenic bacteria develop resistance to the antibiotic drugs, which has been a cause of worry ever since the first antibiotic, penicillin, was developed. It is a need of the hour to develop materials that have an antimicrobial activity that can be used effectively against the strain.

As the threat of emerging pathogens and drug resistance emerges, materials that are biocompatible, economic, and effective against the bacterial strains are needed to be developed. One of the promising alternatives that exhibit remarkable antibacterial activities against several bacteria, including pathogens, is engineered nanomaterials specifically, metal and metal oxide nanoparticles that show remarkable antimicrobial activity [3–5]. They have an excellent antimicrobial activity, which highlights the role of these nanoparticles in several biomedical products [6,7].

10.2 METHODS OF SYNTHESIS OF METAL OXIDES FOR ANTIMICROBIAL ACTIVITY

The method plays a very important role in the synthesis of any material for a particular application. The selection of synthesis method determines many structural and physiochemical properties, such as crystal structure, morphology, size, shape, types of defects, and dispersity of the metal oxides. The metal oxides are synthesized in the following ways:

10.2.1 Biosynthesis Method

Biosynthesis is important since biocompatibility is one of the most important requirements for the nanomaterial to be used in any medicine. Plant-mediated synthesis of nanoparticles (NPs) is a revolutionary technique that has a wide range of applications in agriculture, the food industry, and medicine. Nanoparticles synthesized using conventional methods have limited uses in the medical domain due to their toxicity. Due to the physico-chemical properties of plant-based nanoparticles, the limitations of conventional chemical and physical methods of nanoparticle synthesis have been considerably overcome. ZnO nanoparticles were synthesized from leaf extracts [8–11]. Raliya et al. [12] have synthesized ZnO, MgO, and TiO_2 nanoparticles by using fungus. The major drawbacks of nanoparticle synthesis using biological routes are the less control on the size and shape of nanoparticles, the process can be slow, and after a certain period of time, degradation of synthesized metal oxides can take place. By varying parameters like microorganism type and strain, its growth phase, culture growth medium, pH, substrate concentrations, temperature, reaction time, the addition of non-target ions, and a source compound of the wanted nanoparticle, it is possible to control the size of the particle and their monodispersity [13].

10.2.2 Chemical Method

In the chemical method, the solvent with a high boiling point, other precursors, and surfactants are heated slowly to a high temperature. The major steps in this process are monomer formation and accumulation, nucleation, and growth. The growth process and the boiling point of the solvent control the size and diameter of the particles [14]. CeO_2 nanoparticles were synthesized by chemical method resulting in 25–50 nm size particles. The as-synthesized metal oxide particles were tested against gram-negative and gram-positive bacteria like E. coli, P. aeruginosa, S. pneumoniae, Proteus mirabilis, Klebsiella, and Haemophilus influenzae, S. epidermidis, Enterobacter aerogenes, Citrobacter freundii, and Enterobacter cloacae [15]. ZnO and Vanadium pentoxide (V_2O_5) nanowires with H_2O_2 and Br^- nanoparticles synthesized by this method were tested against gram-negative bacteria like E. coli [16–18].

10.2.3 Microwave Method

The precursors are dissolved in deionized water and stirred to mix well at room temperature till it is jellified. This gel is then irradiated with microwave energy and is cooled at room temperature.

The resulting precipitate is vacuum filtered, washed with deionized water and alcohol, and dried in a vacuum at 80°C for 1 hour. CaO nanoparticles are synthesized by this method resulting in 16 nm particle size and found that the antibacterial effect was more prominent against gram-positive than gram-negative strains [19]. Magnesium oxide nanowires were synthesized using the microwave method and tested for E. coli and Bacillus sp. Bacterial activities showed decreased bacteriostatic activity against E. coli and Bacillus sp. with increasing MgO nanowire concentration [20].

10.2.4 Pyrolytic Method

This method is used to prepare metal oxide nanoparticles by mixing the atomized solution with soluble polymers and preparing a porous matrix before heating the precursor molecules. Due to these steps, the aggregation or agglomeration of nanoparticles is prevented. Cobalt oxide (Co_3O_4) prepared by the pyrolytic method showed antibacterial activity on two bacteria, S. aureus and E. coli [21].

10.2.5 Hydrothermal Method

This method uses an autoclave or steel reactor, which can be kept in an oven/furnace at 120°C–200°C under 2,000 psi pressure. The aqueous solvents can be dissolved and recrystallized in these operating conditions. Different forms of nanoparticles can be obtained by the hydrothermal method by controlling the operating parameters. Quantum dot CdTe conjugated with ZnO was prepared by hydrothermal method and impeded microbial growth of B. subtilis and E. coli and deterred biofilm formation of P. aeruginosa through photocatalytic action [22]. Few layered graphene sheets decorated by ZnO nanoparticles (FLG/ZnO composite) having 20–40 nm size were prepared by Hummers method (graphene oxide) hydrothermal followed by reduction (FLG/ZnO composite). This material exhibited significant antibacterial activity against *S.* Typhi than E. coli [23]. ZnO nanorods were prepared by hydrothermal to check their antimicrobial activity against S. aureus, E. coli, and A. niger microorganisms and inhibited their growth [24].

10.2.6 Sonochemical Method

In the sonochemical method, the solution of the starting material (e.g. metal salts) is subjected to an enhanced ultrasonic vibration to break the chemical bonds of compounds. The ultrasonic waves traveling through a solution cause a change in compression and relaxation. This leads to sound cavitation, which results in the continuous formation, growth, and collapse of foam in the liquid. In addition, the change in pressure creates microscopic bubbles that explode violently leading to the appearance of shock waves in the gas phase deflating the bubble. The effect of the accumulation of millions of deflated bubbles produces a large amount of energy released in the solution. Transient temperature ~5,000 K, pressure ~1,800 atm, and cooling flow greater than 1,010 K/s were recorded at the localized cavitational implosion hotspots [25]. The advantages of the sonochemical method are uniform size distribution, a higher surface area, faster reaction time and improved phase purity of the metal oxide nanoparticles. Using this method, many metal oxides ZnO [26], TiO_2 [27], Fe_3O_4 [28], Mn-doped Fe_2O_3 [29], $PbWO_4$ [30] were synthesized.

10.2.7 Microsynthesis Method

In this method, the precursors are added to a fungal filtrate and by stirring continuously a white precipitate will be formed from a yellowish-brown precipitate. Mycogenesis of cerium oxide nanoparticles using Aspergillus niger culture filtrate resulted in a fine powder that can inhibit the growth of Streptococcus pneumonia, B. subtilis, Proteus Vulgaris, and E. coli. The precipitate of metal oxide nanopowder was obtained using this method and tested against the bacteria. CeO_2 nanoparticles are made by this method [31].

TABLE 10.1
Methods of Synthesis of Metal Oxide Nanoparticles and Some Materials Prepared Using Them

Sr No.	Method of Synthesis	Metal Oxides	References
1	Biosynthesis	ZnO, MgO, TiO_2	[8–13]
2	Microwave	CaO, MgO	[19,20]
3	Pyrolytic	CO_3O_4	[21]
4	Hydrothermal	ZnO, FLG/ZnO	[22–24]
5	Sonochemical	TiO_2, ZnO, $PbWO_4$, Fe_2O_3, Fe_3O_4	[25–30]
6	Mycosynthesis	CeO_2	[31]
7	Combustion/sol-gel combustion	$GdAlO_3$:Eu^{3+}, ZnO, CuO, Fe_2O_3, SAOED/ RB-CF, Ag+/CaTiO3: Pr3+	[35,36,74,77]
8	Chemical	CeO_2, ZnO, V_2O_5, Fe_3O_4, Fe_2-xAgxO_3, CaO,	[15,37–39]

10.2.8 Combustion Method

The combustion synthesis method is used to prepare inorganic phosphors at relatively low temperatures using organic fuels and metal nitrates as oxidizers. The method has many important features like the use of relatively simple equipment, formation of high-purity products, stabilization of metastable phases, and formation of virtually any size and shape of products. These inorganic metal oxides have applications in optoelectronic devices and displays [32–34]. These materials can be used as antimicrobial agents. $GdAlO_3$:Eu^{3+} was synthesized by the combustion method, and it was shown that incorporating Li, K, and Na cations in the host matrix increased the photoluminescence. These materials showed antimicrobial activities against pathogenic microorganisms [35]. A comparative study of CuO, ZnO, and Fe_2O_3 synthesized by the sol-gel combustion method was done. It was found that ZnO nanoparticles were the smallest in size as compared to the other two materials, thereby having the highest surface-to-volume ratio. The antibacterial activity was compared, and it was concluded that the antibacterial activity increased with an increase in surface-to-volume ratio due to a decrease in the size of nanoparticles. The ZnO nanoparticles are more effective against gram-positive bacterial strains compared with gram-negative bacterial strains [36]. Table 10.1 summarizes some of the metal oxides prepared using various methods that are tested for antimicrobial activity.

10.3 MECHANISMS OF METAL OXIDE NANOPARTICLES FOR ANTIMICROBIAL ACTIVITY

Due to the unique physical, chemical, electrical, magnetic, optical, and biological properties, metal oxide nanoparticles are very important to scientists as an antibacterial agent. The mechanism of the antibacterial activity of metal oxide nanoparticles is still in its infancy. Elucidation of the molecular mechanism of metal oxide nanoparticles is now a subject of rigorous research. To investigate possible mechanisms, many studies have been undertaken. The antibacterial activity of metal oxide nanoparticles revealed by recent studies shows that the mechanism is not exhaustive, but research has revealed it as bacterial growth delay/killing. By combining one or more mechanisms, the nature and chemistry of metal oxide nanoparticles can be decided. The main activity is the production of reactive oxygen species (ROS) (Figure 10.1). The other activities are electrostatic interaction, disturbance in metal/metal ion homeostasis, protein and enzyme dysfunction, genotoxicity, and photokilling.

The mechanism of metal oxide nanomaterials interacting with living cells and microorganisms has been widely explored and explained in various ways: The common one is ROS formation. The other mechanisms are interaction with the cell membrane, particle internalization, and binding with specific targets such as proteins or DNA. In oxides, which are made from poly metals, the

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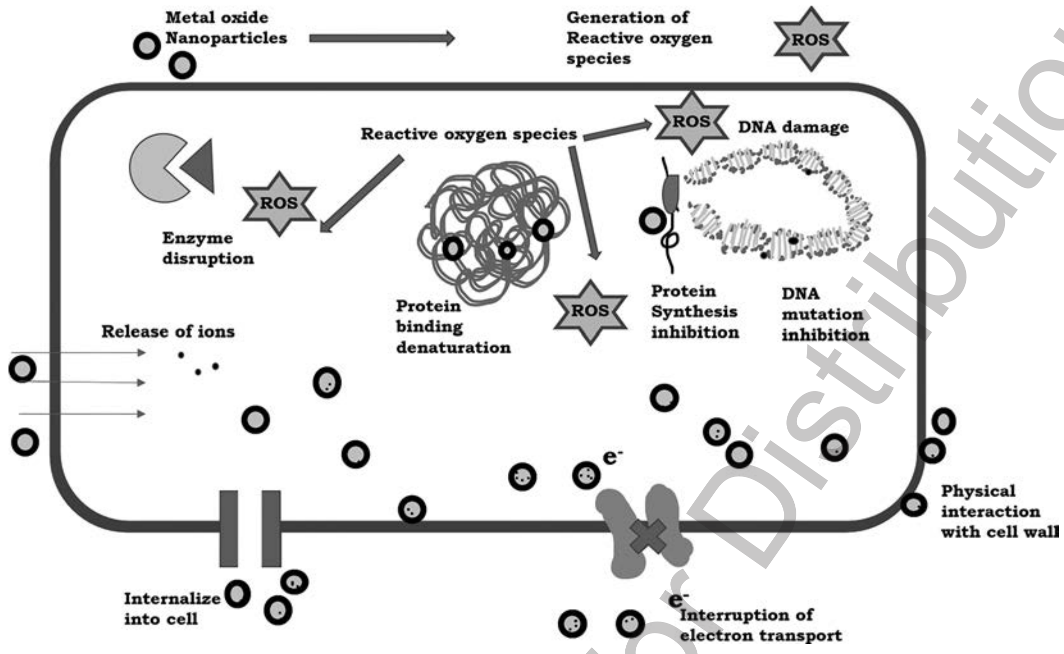

FIGURE 10.1 The plausible mechanisms of metal oxide nanoparticle mediated antimicrobial activities.

physicochemical parameters of the respective components are altered, which can lead to a new reaction in the living organism. Some polymetallic oxide nanoparticles showed little tendency to agglomerate in solutions and biological fluids, resulting in increased antibacterial activity and high biocompatibility for their components.

10.3.1 Bacterial Cell Wall Interaction and Cell Penetration

When bacterial cells are exposed to nanoparticles, it can lead to membrane damage caused by the adsorption of nanoparticles. This is followed by penetration into the cell [40–42]. Many studies suggested that adsorption on the cell wall following its disintegration is the primary mechanism of toxicity [43,44]. Cell wall depolarization takes place and adsorption of NPs makes the cell wall become more permeable. The study by et al. revealed that the bacterial cell wall becomes blurry, indicating cell wall degradation as confirmed by a laser scanning confocal microscope [45].

10.3.2 Oxidative Stress and ROS

Oxidative stress has been confirmed as a key contributor to changing the permeability of the cell membrane, which can result in bacterial cell membrane damage. ROS are highly reactive chemicals formed from O_2. Some of the examples are hydrogen peroxide, hydroxyl radicals, singlet oxygen, and superoxide. This group of molecules has many functions, including antimicrobial activity. ROS are created from metal oxide nanoparticles and help in antibacterial activity. The membrane of bacteria contains phospholipids that can be oxidized by ROS resulting in the destruction of the cell membrane. ROS can damage DNA/RNA and proteins in the cells of bacteria causing the death of bacteria [46–48]. It was discussed in detail that increasing ROS levels in the biosphere represented growing stress levels and thus shaped the evolution of species. If ROS is more than the cell's capacity, oxidative stress comes into the picture. The injuries through oxidative stress in cells are diverse. The damage caused by oxidative stress on the different steps of the central dogma of molecular biology in bacteria is shown in Figure 10.2.

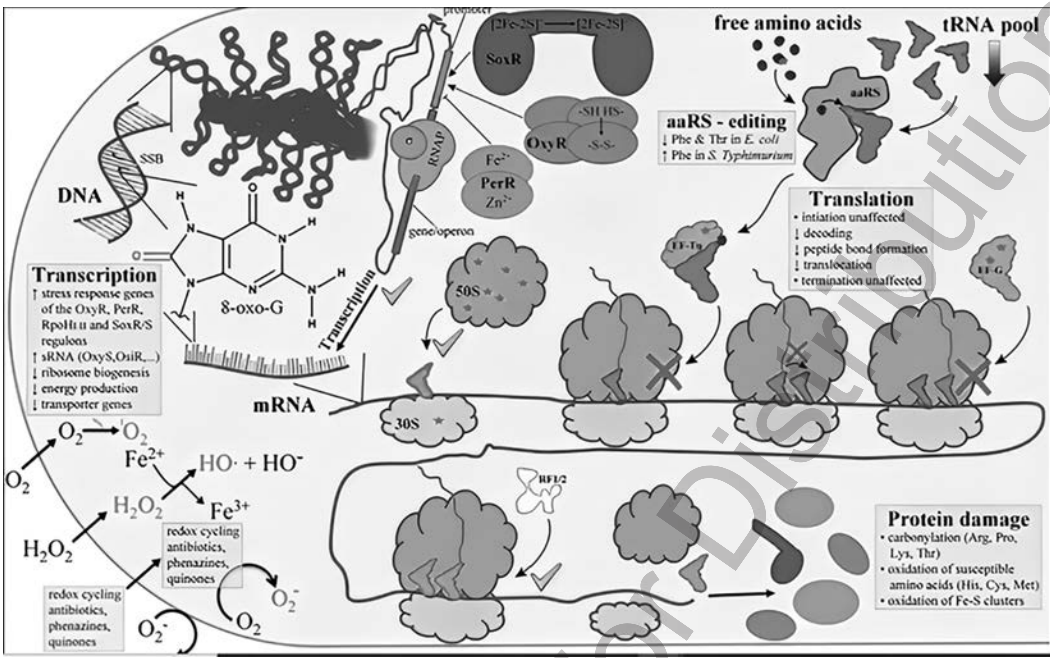

FIGURE 10.2 Damage caused by oxidative stress in bacteria. (Copyright © 2021 Fasnacht and Polacek under Creative Commons Attribution License.)

It was concluded that the central dogma of molecular biology is nonetheless susceptible to oxidative damage, but the pathogens are having their myriad defense mechanisms against ROS [49]. Rai et al. showed that ZnO nanoparticles produced ROS species on the membrane of bacteria cells and showed antibacterial activity against both gram-positive and gram-negative bacteria [50]. The silver nanoparticles and TiO_2 nanoparticles were effectively used as antibacterial agents by Besinis et al. against S. Mutans. They showed that silver nanoparticles have strong antimicrobial activity than chlorhexidine [51]. Xie et al. studied the antibacterial activity of ZnO nanoparticles against Campylobacter jejuni (C. jejuni). They proposed the mechanism of disruption of the cell membrane and oxidative stress in C. jejuni. Their results are significant as the ZnO nanoparticles caused morphological changes, membrane leakage that can be measurable and up to a 52-fold increment in oxidative stress gene expression in C. jejuni [52]. Foster et al. in their work showed that titanium dioxide nanoparticles can adhere to the surface of bacterial cells to produce ROS. These ROS ultimately damage the composition and structure of the cell membrane, in this way interfering with the function of the cell membrane and causing leakage of cellular contents, resulting in bacterial death [53]. MgO nanoparticles are tested against gram-positive and gram-negative bacteria by Sawai et al. They showed that the presence of active oxygen such as superoxide on the surfaces of MgO nanoparticles was the key factor that affects their antibacterial activity [54]. The mixed nanostructure of ZnO-MgO was evaluated by Vidic et al. against both gram-positive and gram-negative bacteria and confirmed that ZnO nanoparticles showed high antimicrobial activity against both, MgO showed moderate and ZnO-MgO mixed phase nanoparticles showed high antimicrobial activity against gram-positive bacteria. They suggested the use of a mixed phase as a new therapeutic for bacterial infection [55].

10.3.3 Electrostatic Interaction

The metal cations separated from metal oxides may get attracted by the negatively charged cell membrane of bacteria and bound to it by electrostatic interactions after which they insert into the hydrophobic core and perturb the structure. This results in an increase in bacterial membrane permeability that induces leakage of cytoplasmic components and consequently the death of bacteria. In this regard, adsorption of metal ions to cell walls is the potential process in destructing bacteria. The metal ions released in the surrounding media get bound with the negatively charged functional groups of the bacterial cell membrane such as phosphate and carboxyl groups. This process is known as biosorption. Different metal ions have shown affinity to different sites; for example, zinc ions showed high affinity towards the –SH groups of proteins. The closely spaced highly ordered cell membranes become confused and dispersed, which destroys their inherent function and leads to bacterial death [56]. Gram-negative bacteria have more negative charge than gram-positive bacteria [57]. Therefore, electrostatic interaction will be stronger in gram-negative bacteria. Lipopolysaccharide (LPS) in the outermost leaflet of the lipid bilayer is the cause of having more charge per unit, thereby making them highly negative in charge [58]. The surface area that is available for interaction also affects the electrostatic force of attraction. The metal oxide nanoparticles are characterized by small size thereby having a large surface area. This feature of metal oxide nanoparticles makes them potential candidates for imparting cytotoxicity. The attachment of a large number of metal oxide nanoparticles alters the structure and permeability of the cell membrane and the strong bond with the membranes results in the disorganization of cell walls. The pores on the membrane are of the order of nanometers and the size of bacteria is of the order of micrometers. The metal oxide nanoparticles enter the cell structure and cause leakage of intracellular contents resulting in the destruction of bacteria [59].

10.3.4 Photokilling

When metal oxide nanoparticles in contact with bacteria are exposed to light, photokilling process takes place. Generation of O_2^- is the main reason, whereas the generation and release of the electron occur through light. The released electrons are grabbed by metal oxide nanoparticles leading to the generation of more ROS. Thus, the effect of light will result in photochemical alteration of the cell membrane, damage to proteins, and abnormal cell division. The photokilling was studied using Fe_3O_4 nanoparticles, and the growth of bacteria was inhibited [60]. UV light was used by another group for photokilling microorganisms using TiO_2 nanoparticles [61]. Pt-dispersed TiO_2 thin film showed excellent photokilling after exposure of UV light for 5 minutes (Figure 10.3) [62].

10.3.5 Protein and Enzyme Dysfunction

The Dysfunctioning of enzymes of a bacterial cell is another mechanism through which the metal oxide nanoparticles carry out antimicrobial activity. Protein-bound carbonyls are the result of catalyzing the oxidation of amino acid side chains by metal oxide nanoparticles. This protein carbonylation will reduce the catalytic activity of enzymes and result in protein degradation. These ions also

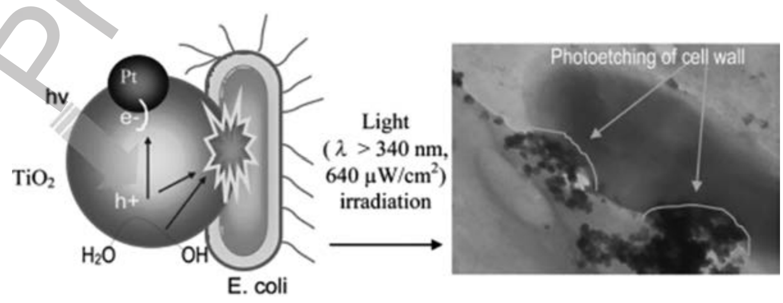

FIGURE 10.3 Photokilling of bacteria using TiO_2 nanoparticles.

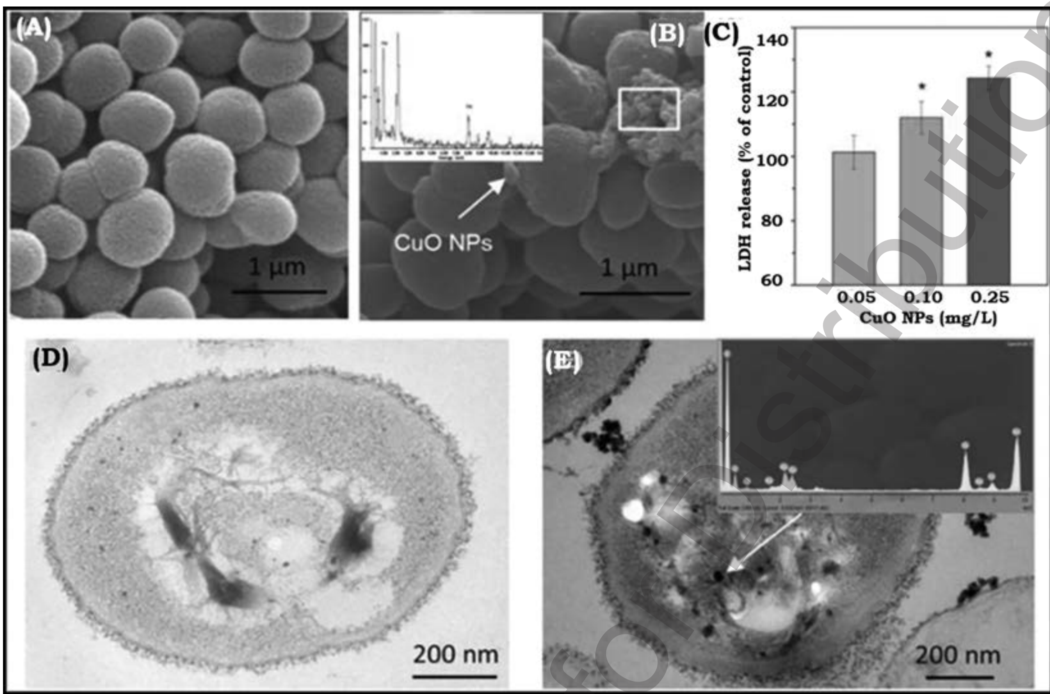

FIGURE 10.4 Effect of CuO NPs on cellular structure of *P. denitrificans.*

react with -SH groups of many proteins and enzymes to make them inactive [63–65]. The influence of CuO nanoparticles on bacterial denitrification was studied by Su et al. as shown in Figure 10.4.

They observed that CuO nanoparticles can alter significantly the expression of key proteins. The proteomic bioinformatics analysis showed that CuO nanoparticles caused the regulation of proteins involved in nitrogen metabolism, electron transfer, and substance transport [66]. This further deteriorates the cell's inner functionalization. The crossing of nanoparticles from the bacteria cell membrane and then damaging the vital enzymes of gram-positive and gram-negative bacteria by highly stabilized CuO nanoparticles were studied [67,68].

10.3.6 Disorder in Metal Ion Homeostasis

For microbial survival, metal ion homeostasis is necessary wherein the metabolic functions are regulated by coenzymes, cofactors, and catalysts. If metal ions are excess in number, it will produce disorder in metabolic functions. As shown in Figure 10.1, when metal ions bind with DNA, its helical structure is disturbed. The copper oxide nanoparticles release copper ions that carry a positive charge, which neutralizes the charges on the LPS and increase the permeability of the outer membrane. The disordered membrane allowed more metal cations to accumulate in the bacterial cell which is reduced to metal atoms by thiol groups (-SH) in enzymes and proteins and hence inactivating the essential proteins blocking, respiration and this leads to cell death [69]. Long-chain polycations were coated on the cell surfaces that kill both gram-positive and gram-negative bacteria [70].

10.4 IMPORTANT AND NEW ERA ANTIMICROBIAL APPLICATIONS

Nanosized metal oxides are widely utilized in skincare merchandise because they have a large spectrum of antimicrobial properties and decreased pores and skin irritation. These nanoparticle-based sunscreens or creams for dermatological packages have already been commercialized. The first sunscreen containing nano-TiO_2 turned commercialized in 1989, and later on, in 1991, ZnO turned into additionally introduced. Furthermore, 70% of TiO_2 sunscreens and 30% of zinc sunscreens contained those ingredients withinside the nanoform [71]. Lancôme Soleil from L'Oréal is one such instance of a nano-based sunscreen. Nanoparticles of ZnO and TiO_2 are frequently utilized in cosmetics; further to the robust antimicrobial hobby, additionally they exhibit physicochemical properties that are beneficial for those cosmetics. The antimicrobial property enables to reflow of odors and protects the pores and skin from colonization via way of means of pathogens. However, permeation through the pores and skin is one of the main worries related to such sunscreens. Various studies have been carried out to determine the penetration capacity of nanoparticles through pores and skin. Permeation of gold and iron oxide nanoparticles particularly with suggest smaller sizes turned into located in a few research. However, the nanoparticles of TiO_2 and ZnO are typically categorized as secure substances for dermal packages. Modern sunscreens contain titanium dioxide (TiO_2) or zinc oxide (ZnO) nanoparticles that are insoluble, colorless, and reflect/disperse ultraviolet (UV) rays more effectively than larger particles. Most of the available theoretical and experimental evidence suggests that insoluble NPs do not penetrate into or through normal or damaged human skin. Oral and topical toxicity data indicate that TiO_2 and ZnO NPs have low systemic toxicity and are well tolerated in the skin [72]. The use of inorganic luminescent particles is being explored for new application areas like the textile industry. For the development of self-disinfecting photodynamic textiles with enhanced antibacterial activity, a facile method has been reported wherein the long-persistent phosphor $SrAl_2O_4$:Eu^{2+}, Dy^{3+} (SAOED) and the photosensitizer rose bengal (RB) onto cotton fabric (CF) are applied by knife coating and photocrosslinking methods (Figure 10.5). The prepared composite material, termed SAOED/RB-CF, showed superior antibacterial efficacy capable of 99.999% (5 log units, detection limit) and 99.986% (3.9 log units) photoinactivation against Staphylococcus aureus and methicillin-resistant S. aureus (MRSA), respectively, under visible light illumination (Xenon lamp). This study suggested that the light emitted from the phosphorescence of the photoexcited SAOED could be absorbed by the rose bengal photosensitizer under

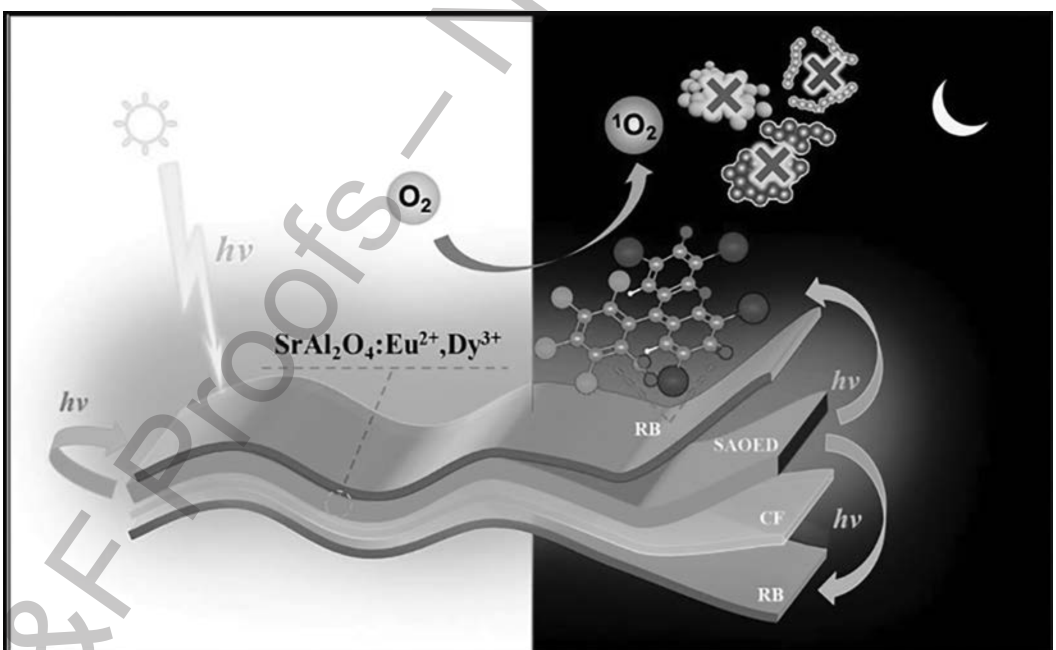

FIGURE 10.5 SAOED/RB-CF shows synergistic antibacterial efficacy by generating singlet oxygen even under dark condition.

dark conditions, resulting in effective synergistic pathogen inactivation [73]. The use of PEGylated palladium-doped CeO_2 for cancerous cell destruction shows a promising application in the field of antimicrobial study. The fluorescent staining results confirmed the cell death in A549 cells through cellular damage by oxidative stress.

The reported material exhibited higher antibacterial activity against bacterial pathogens. Figure 10.6 shows the synthesis, biocompatibility, anticancer activity, and antibacterial activity of PEGylated palladium-doped CeO_2 [74]. A new composite based on aluminum oxide nanoparticles and borosiloxane polymers has been prepared, and its mechanical and physicochemical properties have been studied. The composite inhibits bacteria growth and does not affect the growth of host animal cells. The increase in the concentration of Al_2O_3 nanoparticles showed an increase in cytotoxicity. The reported composite is capable of generating ROS such as hydroxyl radicals and hydrogen peroxide (Figure 10.7). The rate of ROS generation increases threefold with an increase in the concentration of Al_2O_3. It has been shown that the composite can act as a key biomarker of oxidative stress as 8-oxoguanine in DNA [75]. A multifunctional material $CaTiO_3$:Pr^{3+} coated with silver has been prepared and studied for its luminescence and antibacterial properties by Liu et al. They used the sol-gel combustion method for preparing this material. They showed that the emission intensity decreases with the increase in the concentration of Ag^+ in the sample. The reason given for this effect was the special absorptive capacity of Ag^+. When the silver compounds (Band gap 1.46 eV) are irradiated with light having energy more than their band gaps, a separation of valence band electron and conduction band holes is generated. The separated electron hole pairs absorb energy and the energy of Pr^{3+} ions get decreased. Hence, as the activator's energy decreases in luminescent solids, their photoluminescence decreases. They also studied the effect of temperature on the antimicrobial property. The optimized temperature was 800°C. They showed that the antibacterial property increased with increase in the addition of Ag^+ coating. The Ag^+ coated $CaTiO_3$:Pr^{3+} red emitting phosphor excited by ultraviolet radiation thus can be used as a red phosphor in the

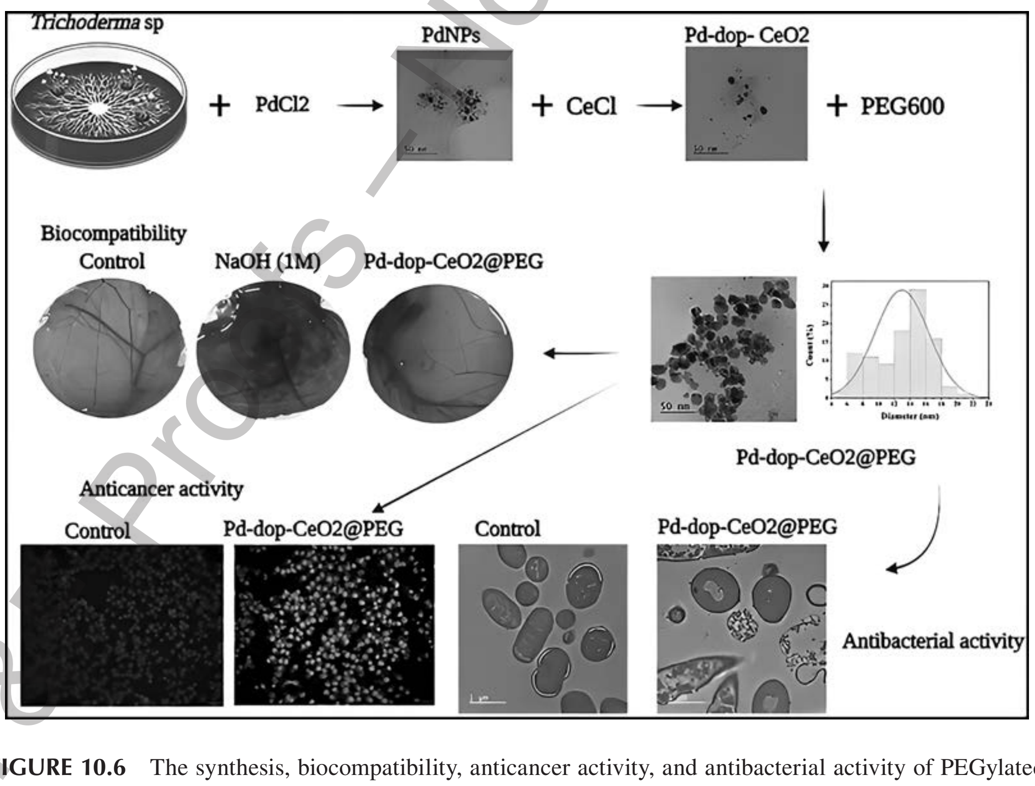

FIGURE 10.6 The synthesis, biocompatibility, anticancer activity, and antibacterial activity of PEGylated palladium-doped CeO_2.

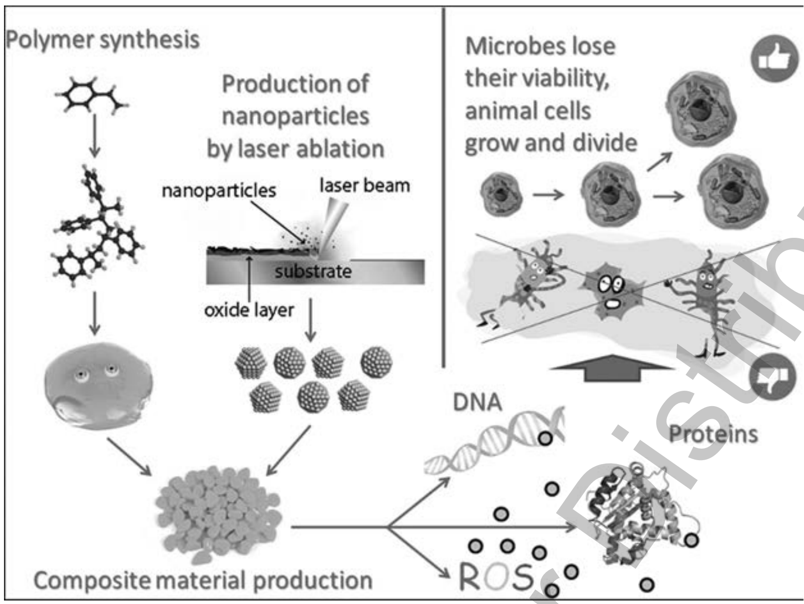

FIGURE 10.7 The composite of polymer and metal oxide nanoparticles inhibiting bacteria growth and not affecting growth of host animal cells by generating ROS.

manufacturing of white light-emitting diodes and antibacterial material as well. This multifunctional material having luminescence and antimicrobial property can be used in medical devices [76]. The facile preparation of traffic warning clothing from long-persistent photoluminescent cotton fabrics has been reported by Khattab et al. They spray-coat a binder with strontium aluminum oxide phosphor ($SrAl_2O_4$:Eu, Dy) in a water environment on cotton fabric. They studied the breathability, flexibility, and comfortability of the coated cotton fabrics and showed that the long-lasting luminescent cotton fabric has the added advantage of being readily visible to the naked eye and its luminescence can be located in the dark. Morphology, surface, and elemental composition, as well as color fastness and luminescence properties of the spray-coated cotton substrates, were explored. They studied the antibacterial and antifungal properties of spray-coated cotton substrates against two gram-negative and gram-positive bacteria, including E. coli and S. aureus, respectively, and Candida albicans fungus by applying the plate agar count methodology, and the antibacterial/antifungal reduction percentage caused by the spray-coated cotton fabrics were calculated. It was observed that the blank cotton fabric showed no inhibition influence on the reduction percentage, but spray-coated fabric showed significant resistance to the pathogens. They rated this microbial resistance ranging from poor to excellent with increasing the concentration of strontium aluminate phosphor. Thus, the reported cotton fabric having antimicrobial properties with the added advantage of glowing in the dark proves additional safety [77].

10.4.1 Antimicrobial Blue Light Applications

Preservation technologies important in the agricultural and medical industries. In this context, light-emitting diode (LED) illumination is widely applied for microbial inactivation. In recent years, LEDs with blue wavelengths are used as an alternative technology to ultraviolet irradiation. Minimally preserved foods such as freshly cut fruits and vegetables that are eaten raw are more prone to contamination by microorganism. This leads to various diseases and food wastage. Moreover, it loses its taste and texture. Consumers prefer the fresh look and smell of minimally processed foods that are preservative-free. To address all these issues in the food industry, thermal

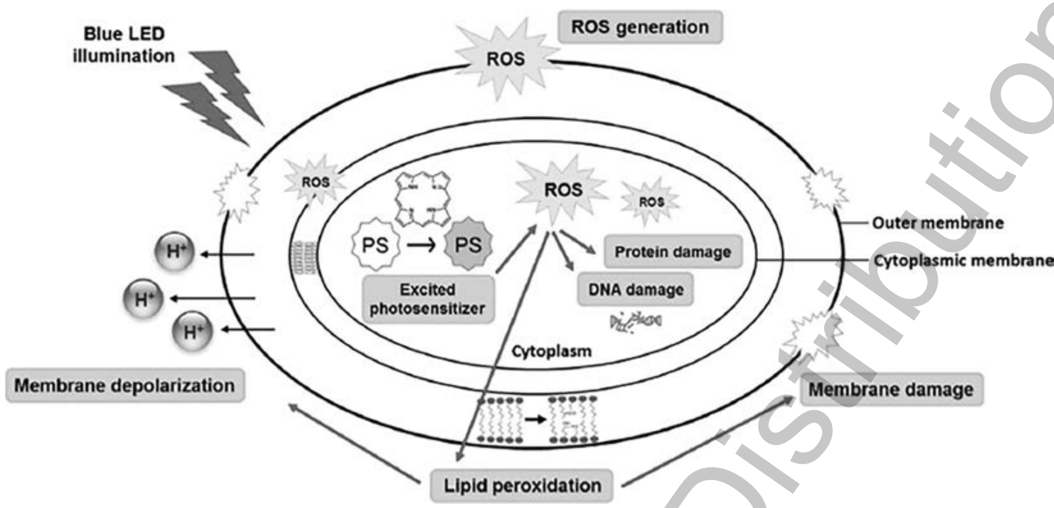

FIGURE 10.8 Antibacterial activity caused by LED illumination.

technology is primarily used for antimicrobial treatment. But the thermal treatment causes loss of nutrition, taste, and texture of fresh produce [78]. To avoid such unwanted effects, nonthermal treatments are explored and are being used for antibacterial treatment for the last 35 years. Among these, light-based technologies have promising potential for foodborne pathogens. The ultraviolet light is generally used for sterilization and in the food packaging industry for its antibacterial effect. But it has a harmful effect on humans for long exposure time and therefore the need arises for the development of safe way for food as well as for people working in the food and agricultural industry [79,80].

LEDs are semiconductor-based light source with a narrowband of emission wavelengths. It can be engineered to emit various colors of light of which the visible range spreads from 400 to 700 nm. The blue, green, and red wavelength regions are used in food industry. LED lights are advantages like more life span, low energy consumption, compact size to name a few as compared to conventional light sources. The LED has been widely used in many applications in the field of postharvest storage, delaying of fruit ripening, cultivation of crops, food preservation, medical therapy and lighting (indoor and outdoor) [81–86]. Blue LEDs exhibit outstanding electrical and optical properties such as high light output power, high brightness, low forward driving voltage, and high internal quantum efficiency (IQE). Figure 10.8 shows the mechanism of LED-driven antibacterial activity.

When the LED light is allowed to fall on the food, it generates ROS, which creates oxidative stress in the membrane of the bacterial cell wall. The possible antibacterial mechanism is that light rays from LEDs excite endogenous photosensitizers such as cytochromes, flavins, NADH, and porphyrins that are naturally present in the cells. This generally results in the formation of ROS, like hydrogen peroxide, hydroxyl radicals, superoxide anions, and singlet oxygen. This process occurs after the absorption of light energy in the presence of oxygen. The cellular components, such as DNA, lipids, and protein, are damaged in this process and eventually lead to the destruction of bacterial cells [87,88]. Also, lipid peroxidation can affect ion pumps in cell membranes and thus increase membrane permeability or depolarization [89]. Table 10.2 shows the effect of blue LED on the killing of microbes studied by various groups in recent years. Along with the illumination time, temperature and intensity of light decide the rate of inhibition of microbes.

10.5 CONCLUSION

Ultraviolet (UV) radiation is a well-known tool for disinfecting food and food surfaces. But, under some conditions, visible light has been proven to have bactericidal characteristics that

TABLE 10.2
Effect of LED Illumination on Various Wavelengths on Pathogenic Bacteria in Foods

Pathogenic Bacteria	Wavelength (nm)	Food	Treatment Time	Temp. (°C)	Result	Reference
S. Montevideo	460	Orange juice	4.9–13.6 hours	4	3.3 log reduction at 4°	[90]
S. Newport				12	3.6 log reduction at 12°	
S. Saintpaul				20	4.8 log reduction at 20°	
S. Gaminara S. Typhimurium C. Jejuni	405	Chicken skin	7.5 hours	10	1.7–2.1 log reduction	[91]
C. coli E. coli	405	Skim milk	90 minutes	5	3.0–5.9 log reduction at 405 nm	[92]
	433			10	2.4–4.1 log reduction at 433 nm	
	460			15	2.8–3.7 log reduction at 460 nm	
S. Montevideo	460	Fresh-cut pineapples	8.7–24 hours	7	0.6–1.0 log reduction at 7°C	[93]
S. Newport				16	0.7–1.7 log reduction at 16°C	
S. Saintpaul				25		
S. Agona	405	Fresh-cut papaya	48 hours	4	1.0–1.2 log reduction at 4°C	[94]
S. Newport				10	0.3–1.3 log reduction at 10°C	
S. Saintpaul				20		
S. Typhimurium						
S. Enteritidis	405	Cooked chicken	48 hours	4	1.0–1.6 log reduction at 4°C	[95]
E. coli O157:H7	405	Fresh-cut mango	48 hours	4	1.0–1.2 log reduction at 4°C	[96]
S. Typhimurium				10		
L. Monocytogenes				20	1.2 log reduction In S. Typhimurium	
E. coli O157:H7	405	Chicken purge	10–20 minutes	10	0.7–1.0 log reduction on chicken purge	[97]
L. Monocytogenes		Chicken skin				
S. Aureus					0.2–0.4 log reduction on chicken skin	
S. saprophyticus Salmonella spp. L. Monocytogenes	460–470	Sliced cheese	168 hours	4	3.6–5.1 log reduction at 4°C	[98]
P. fluorescens			48 hours	25	1.9–2.0 log reduction at 25°C	
L. Monocytogenes	460	Smoked salmon	–	10	1.0 log reduction at 10°C	[99]
E. coli O157:H7	460–470	Fresh-cut apples and cherry tomatoes	5 days	4	<1.48 log reduction at 4°C	[100]

allow it to play an important role in food preservation. In food production, as well as in agriculture and horticulture, the visible light has proven its prime role as it stimulates photosynthesis, which is essential for plant growth and development. The use of visible light is the need of the hour, as the application of low light levels helps the crops retain postharvest quality by reducing senescence and enhancing phytochemical and nutritional content in a variety of species. In the agriculture and food industry, artificial light treatments are being used to disinfect water and food, as well as to enhance plant health and development by employing light energy of various wavelengths. The use of UV and visible range of light spectrum could be the future of non-toxic, chemical-less media for protecting the postharvest produce. The idea could be further implemented in developing the novel applications like germ-free fabrics, food containers, furniture, and everyday gadgets such as home appliances, displays, and mobile phones. For this, there is an urgent need of developing light-emitting metal oxides that can produce ROS that further leads to the inactivation of pathogens. Moreover, the rapid growth and progress in computer-based technology can be integrated with material development, and modern germ-free gadgets can be devised in the near future.

10.6 CHALLENGES AND FUTURE PERSPECTIVES

Due to the innumerable advantages of metal oxide nanoparticles, researchers around the world are making a concerted effort to elucidate the interactions of metal oxides with organisms. But, the mechanism of human toxicity of metal oxide nanoparticles remains to be elucidated. The following characteristics pose a threat to the use of metal oxide nanoparticles as antibacterial agents in humans and other organisms: structure; solubility; the ability to overcome various barriers; synthesis in the system; produces oxidants; the ability to penetrate the nucleus; exposure time; dosage, etc. Before being marketed as an antibacterial agent, it is necessary to assess the risks and side effects. The toxicity of some metal oxide nanoparticles varies with dose and duration of exposure, in addition to cell and tissue types. The primary concern is the prooxidant nature, followed by its potential to damage biomolecules and cell membranes. The microbiological properties of metal oxide nanoparticles depend not only on their physicochemical properties but also on the type of bacterial strain. For this reason, they hold promise as excellent antimicrobial agents for the future and find their place for wide application in nanomedicine. Metal oxides exhibiting antibacterial activities indicate a positive intention to use them as antibacterial agents in medicine as soon as possible. Although technology is developing at a rapid pace, the discovery of new antibiotics is lagging and the worry is that bacteria may become resistant to the drugs at a faster rate than the discovery of new antibiotics. The worldwide spread of MDR bacteria has occurred at a rapid pace as globalization has accelerated in recent years. Various metal oxide nanoparticles exhibiting antibacterial activities against different strains of bacteria and fungi have been extensively reported in recent years.

The rate of development of antibiotic resistance is much faster than the discovery of new antibiotics; To combat the emergence of antibiotic resistance, researchers are constantly searching for new materials such as antibiotic agents. Metal oxide nanoparticles hold great promise in overcoming this microbial resistance. The next obstacle to using metal oxide nanoparticles as antibacterial agents is their potential toxicity to humans. Although they can be an alternative to conventional antibiotics, disruption of beneficial microflora is a concern in addition to systemic toxicity, and effective use needs to be explored. Now it is a matter of knowing the interactions of metal oxide nanoparticles with human cells and organs, such as their ability to cross the blood-brain barrier and the blood-testis barrier. The knowledge gained through research in the coming years will explore metal oxide nanoparticles in agriculture, environmental science, food science, medicine, and veterinary medicine. Bacteria eliminate common and resistant antibiotics via the ATP-binding cassette (ABC) transporter. The entry of divalent metal ions into the cell via the ABC transporter has not been explored by scientists yet. ABC transporters are essential for cell viability and pathogenicity because they participate in transmembrane translocation of essential substrates as well as RNA translation and DNA repair; Any change in these protein systems cannot counteract unwanted changes inside the cell. This requires further investigation of the interaction of metal oxide nanoparticles with the ABC transporter. Nanotechnologists, microbiologists and toxicologists need to find ways to use metal oxide nanoparticles and their assays against specific bacteria. A better understanding of the mechanistic pathways and their safe use will help to modify metal oxide nanoparticles, not only to produce excellent antimicrobials, less toxic to humans, but also to prevent or reduce the undesirable effects on the ecosystem.

The field of nanotechnology should be used wisely for the well-being of mankind without damage to our environment. The adverse effects of use of technology on the surroundings can lead us towards unprecedented situations, which can be avoided through proper precautions and following the safety norms. The use of metal oxide nanoparticles in medicines should be tested in vivo rigorously and should be chosen carefully. The reproducibility with safety concern should be assessed and the toxicity assays should be reported. The clinical studies for various metal oxides should be drafted and accurately evaluated for long term so that critical assessment of the medicine and their effects can be studied. The mechanisms and role of various metal oxides and their applications in every field of life should be monitored and after rigorous testing, they should be used in any product.

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